55, 57, 60, 63, and 65-66 have been amended to eliminate multiple dependency. No new matter has been added.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**Version With Markings to Show Changes Made.**" Also enclosed is a copy of Limited Recognition Under 37 CFR § 10.9(b).

Consideration of the application is now respectfully requested.

Respectfully submitted,

Orest Blaschuk et al.

SEED Intellectual Property Law Group PLLC

Qing Lin, Ph.D.
(See Limited Recognition)

QXL:jab

Enclosures:

Version With Markings to Show Changes Made
Copy of Limited Recognition Under 37 CFR § 10.9(b).

701 Fifth Avenue, Suite 6300
Seattle, Washington 98104-7092
Phone: (206) 622-4900
Fax: (206) 682-6031

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

The following new paragraph has been added to page 1, line 6 before the TECHNICAL FIELD section the following new paragraph:

CROSS-REFERENCE TO RELATED APPLICATION

This application is a continuation of U.S. Patent Application No. 08/939,853, filed September 29, 1997, now issued as U.S. Pat. No. 6,203,788, which application is incorporated herein by reference in its entirety.

In the Claims:

Claims 1-19, 21, 35, 51, 62, 69-188, and 190-192 have been canceled.

Claims 20, 22, 25, 27-29, 33-34, 36-38, 41-43, 46, 50, 52, 54-55, 57, 60, 63, and 65-66 have been amended as follows:

20. (Amended) A method for enhancing the delivery of a drug through the skin of a mammal, comprising contacting epithelial cells of a mammal with a cell adhesion modulating agent and a drug, wherein said modulating agent comprises

(a) the sequence His-Ala-Val, or

(b) an antibody or fragment thereof that specifically binds to a cadherin cell adhesion recognition sequence,

wherein said modulating agent inhibits cadherin-mediated cell adhesion, and wherein the step of contacting is performed under conditions and for a time sufficient to allow passage of said drug across said epithelial cells.

22. (Amended) A method according to claim 20 ~~or claim 21~~, wherein said modulating agent passes into the blood stream of said mammal.

25. (Amended) A method according to claim 20~~ or claim 21~~, wherein said modulating agent further comprises at least one cell adhesion recognition sequence bound by an adhesion molecule other than a classical cadherin, and wherein said cell adhesion recognition sequence is separated from any His-Ala-Val sequence(s) by a linker.

27. (Amended) A method according to claim 20~~ or claim 21~~, wherein said modulating agent is linked to a targeting agent.

28. (Amended) A method according to claim 20~~ or claim 21~~, wherein said modulating agent is linked to said drug.

29. (Amended) A method according to claim 20~~ or claim 21~~, wherein said modulating agent is present within a pharmaceutical composition comprising a pharmaceutically acceptable carrier.

33. (Amended) A method according to claim 20~~ or claim 21~~, wherein the step of contacting is performed via a skin patch comprising said modulating agent and said drug.

34. (Amended) A method for enhancing the delivery of a drug to a tumor in a mammal, comprising administering to a mammal a cell adhesion modulating agent and a drug, wherein said modulating agent comprises

(a) 3-16 amino acid residues, including the sequence His-Ala-Val, or

(b) an antibody or fragment thereof that specifically binds to a cadherin cell adhesion recognition sequence,

and wherein said modulating agent inhibits cadherin-mediated cell adhesion.

36. (Amended) A method according to claim 34~~ or claim 35~~, wherein the tumor is selected from the group consisting of bladder tumors, ovarian tumors and melanomas.

37. (Amended) A method according to claim 34 ~~or claim 35~~, wherein said composition is administered to said tumor.

38. (Amended) A method according to claim 34 ~~or claim 35~~, wherein said composition is administered systemically.

41. (Amended) A method according to claim 34 ~~or claim 35~~, wherein said modulating agent is linked to a targeting agent.

42. (Amended) A method according to claim 34 ~~or claim 35~~, wherein said modulating agent linked to said drug.

43. (Amended) A method according to claim 34 ~~or claim 35~~, wherein said modulating agent further comprises one or more of:

(a) a cell adhesion recognition sequence bound by an adhesion molecule other than a classical cadherin, wherein said cell adhesion recognition sequence is separated from any His-Ala-Val sequence(s) by a linker; and/or

(b) an antibody or antigen-binding fragment thereof that binds to a cell adhesion recognition sequence bound by an adhesion molecule other than a classical cadherin.

46. (Amended) A method according to claim 33 ~~or claim 34~~, wherein said modulating agent and said drug are present within a pharmaceutical composition comprising a pharmaceutically acceptable carrier.

50. (Amended) A method for treating cancer in a mammal, comprising administering to a mammal a cell adhesion modulating agent, wherein said modulating agent comprises

(a) 3-16 amino acid residues, including the sequence His-Ala-Val, or

(b) an antibody or fragment thereof that specifically binds to a cadherin cell adhesion recognition sequence.

and wherein said modulating agent inhibits cadherin-mediated cell adhesion.

52. (Amended) A method according to claim 50 ~~or claim 51~~, wherein said cancer is selected from the group consisting of carcinomas, leukemia and melanomas.

54. (Amended) A method according to claim 50 ~~or claim 51~~, wherein said modulating agent is linked to a targeting agent.

55. (Amended) A method according to claim 50 ~~or claim 51~~, wherein said modulating agent further comprises at least one cell adhesion recognition sequence bound by an adhesion molecule other than a classical cadherin, and wherein said cell adhesion recognition sequence is separated from any His-Ala-Val sequence(s) by a linker.

57. (Amended) A method according to claim 50 ~~or claim 51~~, wherein said modulating agent is present within a pharmaceutical composition comprising a pharmaceutically acceptable carrier.

60. (Amended) A method for inhibiting angiogenesis in a mammal, comprising administering to a mammal a cell adhesion modulating agent, wherein said modulating agent comprises

(a) the sequence His-Ala-Val,

(b) an antibody or fragment thereof that specifically binds to a cadherin cell adhesion recognition sequence,

and wherein said modulating agent inhibits cadherin-mediated cell adhesion.

63. (Amended) A method according to claim 60 ~~or claim 62~~, wherein said modulating agent further comprises at least one cell adhesion recognition sequence bound by an adhesion molecule other than a classical cadherin, and wherein said cell adhesion recognition sequence is separated from any His-Ala-Val sequence(s) by a linker.

65. (Amended) A method according to claim 60~~ or claim 62~~, wherein said modulating agent is linked to a target agent.

66. (Amended) A method according to claim 60~~ or claim 62~~, wherein said modulating agent is present within a pharmaceutical composition comprising a pharmaceutically acceptable carrier.

D:\NrPortbl\iManage\JUDIB\303978_1.DOC

#10

EXPRESS MAIL NO. EL897865300US


**BEFORE THE OFFICE OF ENROLLMENT AND DISCIPLINE**
**UNITED STATE PATENT AND TRADEMARK OFFICE**

## LIMITED RECOGNITION UNDER 37 CFR § 10.9(b)

Qing Lin is hereby given limited recognition under 37 CFR § 10.9(b) as an employee of the Seed Intellectual Property Law Group PLLC. law firm to prepare and prosecute patent applications wherein the patent applicant is the client of the Seed Intellectual Property Law Group PLLC. law firm, and the attorney or agent of record in the applications is a registered practitioner who is a member of the Seed Intellectual Property Law Group PLLC. law firm. This limited recognition shall expire on the date appearing below, or when whichever of the following events first occurs prior to the date appearing below: (i) Qing Lin ceases to lawfully remain and reside in the United States, (ii) Qing Lin's employment with the Seed Intellectual Property Law Group PLLC. law firm ceases or is terminated, or (iii) Qing Lin's current Employment Authorization card expires.

This document constitutes proof of such recognition. The original of this document is on file in the Office of Enrollment and Discipline of the U.S. Patent and Trademark Office.

**Expires: May 17, 2003**

Harry I. Moatz
Director of Enrollment and Discipline